THE SYNTHESIS OF 4-ISOPROPENYLCYCLOHEXANONE

BY

ROY HENDERSON BIBLE, JR.

B.S., Virginia Polytechnic Institute, 1948
M.S., University of Illinois, 1949

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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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Introduction

Considerable confusion persists in the literature as to the occurrence and interchangeability of isopropenyl-isopropylidene isomers in the terpene series. The multiplicity of approaches to the problem has, in most cases, only led to more confusion, since different methods have led to conflicting results. The eventual success of any attempt to bring clarity to the various aspects of the isopropenyl-isopropylidene problem depends ultimately on the availability of the pure isomers.

The synthesis of 4-isopropenylcyclohexanone was unsuccessfully attempted by McPherson[1] in an effort to provide a general approach to the total synthesis of a number of terpenes belonging to the 8(9)-*p*-menthene series. Berry[2] later studied the isopropenyl-isopropylidene rearrangement using 8(9)-*p*-menthene under various conditions which would probably be involved in terpene syntheses starting with 4-isopropenylcyclohexanone.

In addition to its possible value as an intermediate in terpene syntheses, 4-isopropenylcyclohexanone should also serve as a useful compound in the study of the isopropenyl-isopropylidene rearrangement.

Although two previous claims[3,4] to the synthesis of 4-isopropenylcyclohexanone have been made, both of the methods used could have led to a mixture of isomers.

Discussion Of Results

The first unequivocal synthesis of 4-isopropenylcyclohexanone has been accomplished in the following manner. Hydroquinone was hydrogenated to give *cis*-1,4-dihydroxycyclohexane. The monobenzyl ether of *cis*-1,4-dihydroxycyclohexane was prepared by treating the monosodium salt of the

glycol with benzyl chloride. 4-Benzyloxycyclohexanol was oxidized with chromic acid to give 4-benzyloxycyclohexanone. The 2,4-dinitrophenylhydrazone of 4-benzyloxycyclohexanone was prepared. Ethyl α-(4-benzyloxy-1-hydroxycyclohexyl)-propionate was prepared by condensing 4-benzyloxycyclohexanone and ethyl α-bromopropionate in the presence of zinc. Ethyl α-(4-benzyloxy-1-hydroxycyclohexyl) propionate was dehydrated (1) by refluxing it with a mixture of acetic anhydride and acetyl chloride, or (2) by heating it with a small amount of iodine followed by distillation over a small amount of sulfuric acid, or (3) by heating it with a combination of small amounts of iodine and sulfuric acid. It was shown by absorption spectra that each of these methods of dehydration gave ethyl α-(4-benzyloxy-1-cyclohexenyl) propionate. The use of acetic anhydride and acetyl chloride led occasionally to the cleavage of the benzyl ether. Ethyl α-(4-benzyloxy-1-cyclohexenyl) propionate was reduced by lithium aluminum hydride to give β-(4-benzyloxy-1-cyclohexenyl)-*n*-propyl alcohol which was then acetylated by acetic anhydride and a trace of acetyl chloride. When distilled under reduced pressure from any apparatus other than a small, short-path distillation apparatus, the acetate of β-(4-benzyloxy-1-cyclohexenyl)-*n*-propyl alcohol partially decomposed to give 2-(4-benzyloxy-1-cyclohexenyl)-propylene. This substituted butadiene was reduced over palladium. The product of this reduction, 4-isopropylcyclohexanol, was oxidized with chromic acid to give 4-isopropylcyclohexanone, which was identified by its 2,4-dinitrophenylhydrazone. β-(4-Benzyloxy-1-cyclohexenyl)-*n*-propyl acetate, which was shown to be resistant to hydrogenolysis over Raney nickel, was reduced over palladium on charcoal to give β-(4-hydroxycyclohexyl)-*n*-propyl acetate. β-(4-Ketocyclohexyl)-*n*-propyl acetate, which was obtained by a chromic acid oxidation of β-(4-hydroxycyclohexyl)-*n*-propyl acetate, was pyrolyzed to give 4-isopropenylcyclohexanone. The infrared absorption spectrum of 4-isopropenylcyclohexanone was determined.

The following compounds which were isolated in pure form

in this series have not been previously reported: 4-benzyloxycyclohexanol, 4-benzyloxycyclohexanone and its 2,4-dinitrophenylhydrazone, ethyl α-(4-benzyloxy-1-cyclohexenyl)propionate, β-(4-benzyloxy-1-cyclohexenyl)-*n*-propyl alcohol and β-(4-hydroxycyclohexyl)-*n*-propyl acetate.

BIBLIOGRAPHY

1. McPherson, Thesis, Doctor of Philosophy, University of Illinois, 1948.
2. Berry, Thesis, Doctor of Philosophy, University of Illinois, 1949.
3. Perkin, J. Chem. Soc., 85, 659 (1904).
4. Semmler and Hoffmann, Ber., 37, 239 (1904).

VITA

Roy Henderson Bible, Jr. was born at Roanoke, Virginia on May 31, 1926. After being graduated from William Fleming High School in 1944, he enlisted in the Army and subsequently attended the Virginia Military Institute at Lexington, Virginia, and the University of Maine at Orono, Maine. Upon being discharged from the Army in 1946, he enrolled at the Virginia Polytechnic Institute where he received the degree of Bachelor of Science in Chemistry in 1948. During the summer of 1948 he was employed as a chemist by Tennessee Eastman Corporation, Kingsport, Tennessee. In September of that year he entered the Graduate College of the University of Illinois and completed the requirements for the degree of Master of Science in Chemistry in August, 1949. He held Teaching Assistantships from September, 1949, to June, 1951, and a Marsh Fund Research Grant from the National Academy of Sciences during the summer of 1951. On June 10, 1951, he was married to Harriett V. Bertoglio of Benld, Illinois. The author is a member of Alpha Chi Sigma, Sigma Xi, and Phi Lambda Upsilon.